THE AMERICAN JOURNAL OF HUMAN GENETICS

EDITOR
Peter H. Byers, M.D.
University of Washington
School of Medicine
Seattle, WA

MANAGING EDITOR
Roberta Wilkes
University of Washington
Seattle, WA

ASSOCIATE MANAGING EDITOR
Patricia Baskin
University of Washington
Seattle, WA

ASSOCIATE EDITORS

Gregory S. Barsh, M.D., Ph.D.
Stanford University Medical
Center
Stanford, CA

Anne M. Bowcock, Ph.D.
University of Texas Southwestern
Medical Center
Dallas, TX

Diane W. Cox, Ph.D.
The Hospital for Sick Children
Toronto, Ontario

Thomas W. Glover, Ph.D.
University of Michigan
Ann Arbor, MI

Markus Grompe, M.D.
Oregon Health Sciences
University
Portland, OR

James R. Lupski, M.D., Ph.D.
Baylor College of Medicine
Houston, TX

Kenneth Morgan, Ph.D.
McGill University
Montreal, Quebec

Roberta A. Pagon, M.D.
University of Washington
Seattle, WA

Richard S. Spielman, Ph.D.
University of Pennsylvania
Philadelphia, PA

Barbara L. Weber, M.D.
University of Pennsylvania
Philadelphia, PA

James L. Weber, Ph.D.
Marshfield Medical Research
Foundation
Marshfield, WI

Daniel E. Weeks, Ph.D.
University of Pittsburgh
Pittsburgh, PA
The Wellcome Trust Centre for
Human Genetics
Oxford

Volume 61
1997

Published Monthly for
THE AMERICAN SOCIETY OF HUMAN GENETICS
BY THE UNIVERSITY OF CHICAGO PRESS

THE AMERICAN SOCIETY OF HUMAN GENETICS

BOARD OF DIRECTORS

President
Larry J. Shapiro, M.D.
University of California,
San Francisco
San Francisco, CA

President-Elect
Arthur L. Beaudet, M.D.
Baylor College of Medicine
Houston, TX

Secretary
Ann C. M. Smith, M.A.
Georgetown University
Washington, DC

Treasurer
Stephen I. Goodman, M.D.
University of Colorado Health
Sciences Center
Denver, CO

Editor
Peter H. Byers, M.D.
University of Washington
School of Medicine
Seattle, WA

President 1995
Judith G. Hall, M.D.
University of British Columbia
Vancouver, BC

President 1996
Charles J. Epstein, M.D.
University of California,
San Francisco
San Francisco, CA

Directors

Diane Baker, M.S.
University of Michigan
Ann Arbor, MI

John C. Carey, M.D.
University of Utah Medical Center
Salt Lake City, UT

Aravinda Chakravarti, Ph.D.
Case Western Reserve University
School of Medicine
Cleveland, OH

Michael R. Hayden, M.D., Ph.D.
University of British Columbia
Vancouver, BC

Judith H. Miles, M.D., Ph.D.
University of Missouri Hospital
Columbia, MO

Jeffrey C. Murray, M.D.
University of Iowa
Iowa City, IA

Philip R. Reilly, M.D., J.D.
Shriver Center for Mental
Retardation, Inc.
Waltham, MA

Stephanie L. Sherman, Ph.D.
Emory University School of
Medicine
Atlanta, GA

Stephen T. Warren, Ph.D.
Emory University School of
Medicine
Atlanta, GA

© 1997 by The American Society of Human Genetics

Contents of Volume 61

July 1997

i **This Month in the *Journal***
John Ashkenas

Invited Editorials

1 **Human Female Meiosis: New Insights into an Error-Prone Process**
Dorothy Warburton

5 ***XIST* Expression and X-Chromosome Inactivation in Human Preimplantation Embryos**
Carolyn J. Brown and Wendy P. Robinson

9 **When Is a Deletion Not a Deletion? When It Is Converted**
Arthur H. M. Burghes

16 **Multilocus FISH Analysis**
Roberta A. Pagon

Commentary and Invited Correspondence

18 **COMMENTARY: Homologous Recombination in Human Mitochondria?**
John Ashkenas

19 **INVITED CORRESPONDENCE: mtDNA Recombination: What Do In Vitro Data Mean?**
Neil Howell

Original Articles

23 **First-Meiotic-Division Nondisjunction in Human Oocytes**
Roslyn Angell

33 ***XIST* Expression in Human Oocytes and Preimplantation Embryos**
R. Daniels, M. Zuccotti, T. Kinis, P. Serhal, and M. Monk

40 **Genomic Variation and Gene Conversion in Spinal Muscular Atrophy: Implications for Disease Process and Clinical Phenotype**
Louise Campbell, Allyson Potter, Jaakko Ignatius, Victor Dubowitz, and Kay Davies

51 **Simultaneous, Multilocus FISH Analysis for Detection of Microdeletions in the Diagnostic Evaluation of Developmental Delay and Mental Retardation**
Azra H. Ligon, Arthur L. Beaudet, and Lisa G. Shaffer

60 **The Activin Receptor–Like Kinase 1 Gene: Genomic Structure and Mutations in Hereditary Hemorrhagic Telangiectasia Type 2**
Jonathan N. Berg, Carol J. Gallione, Timothy T. Stenzel, David W. Johnson, William P. Allen, Charles E. Schwartz, Charles E. Jackson, Mary E. M. Porteous, and Douglas A. Marchuk

68 **Characterization of Endoglin and Identification of Novel Mutations in Hereditary Hemorrhagic Telangiectasia**
Claire L. Shovlin, J. M. B. Hughes, J. Scott, Christine E. Seidman, and J. G. Seidman

80 **Constitutively Methylated CpG Dinucleotides as Mutation Hot Spots in the Retinoblastoma Gene (RB1)**
Debora Mancini, Shiva Singh, Peter Ainsworth, and David Rodenhiser

88 **Different Mechanisms and Recurrence Risks of Imprinting Defects in Angelman Syndrome**
Joachim Bürger, Karin Buiting, Bärbel Dittrich, Stephanie Groß, Christina Lich, Karl Sperling, Bernhard Horsthemke, and André Reis

94 **Definitive Evidence for an Autosomal Recessive Form of Hypohidrotic Ectodermal Dysplasia Clinically Indistinguishable from the More Common X-Linked Disorder**
F. Munoz, G. Lestringant, V. Sybert, M. Frydman, A. Alswaini, P. M. Frossard, R. Jorgenson, and J. Zonana

101 **Phenotype Correlation and Intergenerational Dynamics of the Friedreich Ataxia GAA Trinucleotide Repeat**
Eugènia Monrós, Maria Dolores Moltó, Francisco Martínez, Joaquín Cañizares, José Blanca, Juan J. Vílchez, Félix Prieto, Rosa de Frutos, and Francesc Palau

111 **Identification of the Human Chromosomal Region Containing the Iridogoniodysgenesis Anomaly Locus by Genomic-Mismatch Scanning**
Farideh Mirzayans, Alan J. Mears, Sun-Wei Guo, William G. Pearce, and Michael A. Walter

120 **Cancer Risks in Two Large Breast Cancer Families Linked to BRCA2 on Chromosome 13q12-13**
D. F. Easton, L. Steele, P. Fields, W. Ormiston, D. Averill, P. A. Daly, R. McManus, S. L. Neuhausen, D. Ford, R. Wooster, L. A. Cannon-Albright, M. R. Stratton, and D. E. Goldgar

129 **Reduced Frequency of Extracolonic Cancers in Hereditary Nonpolyposis Colorectal Cancer Families with Monoallelic *hMLH1* Expression**
Anne Charlotte Jäger, Marie Luise Bisgaard, Torben Myrhøj, Inge Bernstein, Jens F. Rehfeld, and Finn Cilius Nielsen

139 **Linkage of Niemann-Pick Disease Type D to the Same Region of Human Chromosome 18 as Niemann-Pick Disease Type C**
W. L. Greer, D. C. Riddell, D. M. Byers, J. P. Welch, G. S. Girouard, S. M. Sparrow, T. L. Gillan, and P. E. Neumann

143 **The Locus for Combined Factor V–Factor VIII Deficiency (F5F8D) Maps to 18q21, between D18S849 and D18S1103**
M. Neerman-Arbez, S. E. Antonarakis, J.-L. Blouin, S. Zeinali, M. Akhtari, Y. Afshar, and E. G. D. Tuddenham

151 **The Seventh Form of Autosomal Recessive Limb-Girdle Muscular Dystrophy Is Mapped to 17q11-12**
Eloisa S. Moreira, Mariz Vainzof, Sueli K. Marie, Andrea L. Sertié, Mayana Zatz, and Maria R. Passos-Bueno

160 **Familial Skewed X Inactivation: A Molecular Trait Associated with High Spontaneous-Abortion Rate Maps to Xq28**
Elena Pegoraro, Jeanette Whitaker, Patricia Mowery-Rushton, Urvashi Surti, Mark Lanasa, and Eric P. Hoffman

171 **Evidence That the Apolipoprotein E–Genotype Effects on Lipid Levels Can Change with Age in Males: A Longitudinal Analysis**
Gail P. Jarvik, Ellen L. Goode, Melissa A. Austin, Johan Auwerx, Samir Deeb, Gerard D. Schellenberg, and Terry Reed

182 **$Fc_{\varepsilon}R1$-β Polymorphism and Total Serum IgE Levels in Endemically Parasitized Australian Aborigines**
L. J. Palmer, P. D. Paré, J. A. Faux, M. F. Moffatt, S. E. Daniels, P. N. LeSouëf, P. R. Bremner, E. Mockford, M. Gracey, R. Spargo, A. W. Musk, and W. O. C. M. Cookson

189 **Testing Association between Candidate-Gene Markers and Phenotype in Related Individuals, by Use of Estimating Equations**
David-Alexandre Trégouët, Pierre Ducimetière, and Laurence Tiret

200 **A Linkage Strategy for Detection of Human Quantitative-Trait Loci. I. Generalized Relative Risk Ratios and Power of Sib Pairs with Extreme Trait Values**
Chi Gu and D. C. Rao

211 **A Linkage Strategy for Detection of Human Quantitative-Trait Loci. II. Optimization of Study Designs Based on Extreme Sib Pairs and Generalized Relative Risk Ratios**
Chi Gu and D. C. Rao

223 **Variable Age at Onset in Insulin-Dependent Diabetes Mellitus, by the Marker-Association-Segregation-χ^2 Method**
Noël Bonneuil, Antoine Clerget, and Françoise Clerget-Darpoux

Letters to the Editor

228 **Inter- and Intrachromosomal Rearrangements Are Both Involved in the Origin of 15q11-q13 Deletions in Prader-Willi Syndrome**
Romeo Carrozzo, Elena Rossi, Susan L. Christian, Kirk Kittikamron, Chiara Livieri, Andrea Corrias, Lucia Pucci, Alberto Fois, Paolo Simi, Laura Bosio, Luciano Beccaria, Orsetta Zuffardi, and David H. Ledbetter

231 **DNA Studies of Limb-Girdle Muscular Dystrophy Type 2A in the Amish Exclude a Modifying Mitochondrial Gene and Show No Evidence for a Modifying Nuclear Gene**
V. M. Pratt, C. E. Jackson, D. C. Wallace, D. S. Gurley, A. Feit, and G. L. Feldman

233 **A C2055T Transition in Exon 8 of the ATP7A Gene Is Associated with Exon Skipping in an Occipital Horn Syndrome Family**
Nathalie Ronce, Marie-Pierre Moizard, Laura Robb, Annick Toutain, Laurent Villard, and Claude Moraine

238 **Nonreplication of Linkage Disequilibrium between the Dopamine D4 Receptor Locus and Tourette Syndrome**
Johannes Hebebrand, Markus M. Nöthen, Andreas Ziegler, Birgit Klug, Helge Neidt, Katja Eggermann, Gerd Lehmkuhl, Fritz Poustka, Martin H. Schmidt, Peter Propping, and Helmut Remschmidt

239 **Exclusion of Atypical Vitelliform Macular Dystrophy from 8q24.3 and from Other Known Macular Degenerative Loci**
Melanie M. Sohocki, Lori S. Sullivan, Helen A. Mintz-Hittner, Kent Small, Robert E. Ferrell, and Stephen P. Daiger

241 **Diagnostic Testing for Prader-Willi and Angelman Syndromes: Response**
Arabella Smith, Tina Buchholz, and Lisa Robson

244 **Further Comments on the Characterization of Founder Amerindian Mitochondrial Haplotypes**
Néstor O. Bianchi and Graciela Bailliet

246 **Reply to Bianchi and Bailliet**
Peter Forster, Rosalind Harding, Antonio Torroni, and Hans-Jürgen Bandelt

247 **Paleolithic and Neolithic Lineages in the European Mitochondrial Gene Pool**
L. L. Cavalli-Sforza and E. Minch

251 **Reply to Cavalli-Sforza and Minch**
Martin Richards, Vincent Macaulay, Bryan Sykes, Paul Pettitt, Robert Hedges, Peter Forster, and Hans-Jürgen Bandelt

254 **Nonparametric Linkage Tests Are Model Free**
Leonid Kruglyak

Announcements

256 **Employment and Fellowship Opportunities; Meeting; Courses; Calls for Patients; Cell Cultures and Samples Available; NIDDM Genetic Database**

Information for Contributors

August 1997

i **This Month in the *Journal***
John Ashkenas

Gene Regulation '97

259 **The Regulation of Splice-Site Selection, and Its Role in Human Disease**
Thomas A. Cooper and William Mattox

267 **The Final Stage of Gene Expression: Chaperones and the Regulation of Protein Fate**
John Ashkenas and Peter H. Byers

Insights from Model Systems

273 **Embryonic Lethal Abnormal Visual RNA-Binding Proteins Involved in Growth, Differentiation, and Posttranscriptional Gene Expression**
Dragana Antic and Jack D. Keene

Invited Editorial

279 **Predictive Testing for Retinoblastoma Comes of Age**
Brenda L. Gallie

Original Articles

282 **Constitutional RB1-Gene Mutations in Patients with Isolated Unilateral Retinoblastoma**
Dietmar R. Lohmann, Martin Gerick, Birgit Brandt, Ulrich Oelschläger, Birgit Lorenz, Eberhard Passarge, and Bernhard Horsthemke

295 **Coding Mutations in $p57^{KIP2}$ Are Present in Some Cases of Beckwith-Wiedemann Syndrome but Are Rare or Absent in Wilms Tumors**
Denise O'Keefe, Diem Dao, Long Zhao, Rhonda Sanderson, Dorothy Warburton, Lawrence Weiss, Kwame Anyane-Yeboa, and Benjamin Tycko

304 **Low Frequency of $p57^{KIP2}$ Mutation in Beckwith-Wiedemann Syndrome**
Maxwell P. Lee, Michael DeBaun, Gurvaneet Randhawa, Betty A. Reichard, Stephen J. Elledge, and Andrew P. Feinberg

310 **Spectrum of Mutations in the Batten Disease Gene, *CLN3***
Patricia B. Munroe, Hannah M. Mitchison, Angela M. O'Rawe, John W. Anderson, Rose-Mary Boustany, Terry J. Lerner, Peter E. M. Taschner, Nanneke de Vos, Martijn H. Breuning, R. Mark Gardiner, and Sara E. Mole

317 **Identification and Analysis of Mutations in the Wilson Disease Gene (*ATP7B*): Population Frequencies, Genotype-Phenotype Correlation, and Functional Analyses**
Anjali B. Shah, Igor Chernov, Hong Tao Zhang, Barbara M. Ross, Kamna Das, Svetlana Lutsenko, Enrico Parano, Lorenzo Pavone, Oleg Evgrafov, Irina A. Ivanova-Smolenskaya, Göran Annerén, Kerstin Westermark, Francisco Hevia Urrutia, Graciela K. Penchaszadeh, Irmin Sternlieb, I. Herbert Scheinberg, T. Conrad Gilliam, and Konstantin Petrukhin

329 **Hereditary Nonpolyposis Colorectal Cancer Families Not Complying with the Amsterdam Criteria Show Extremely Low Frequency of Mismatch-Repair-Gene Mutations**
Juul Wijnen, P. Meera Khan, Hans Vasen, Heleen van der Klift, Adri Mulder, Inge van Leeuwen-Cornelisse, Bert Bakker, Monique Losekoot, Pål Møller, and Riccardo Fodde

336 **Japanese Families with Autosomal Dominant Pure Cerebellar Ataxia Map to Chromosome 19p13.1-p13.2 and Are Strongly Associated with Mild CAG Expansions in the Spinocerebellar Ataxia Type 6 Gene in Chromosome 19p13.1**
K. Ishikawa, H. Tanaka, M. Saito, N. Ohkoshi, T. Fujita, K. Yoshizawa, T. Ikeuchi, M. Watanabe, A. Hayashi, Y. Takiyama, M. Nishizawa, I. Nakano, K. Matsubayashi, M. Miwa, S. Shoji, I. Kanazawa, S. Tsuji, and H. Mizusawa

347 **Linkage Analysis of 49 High-Risk Families Does Not Support a Common Familial Prostate Cancer–Susceptibility Gene at 1q24-25**
Richard A. McIndoe, Janet L. Stanford, Mark Gibbs, Gail P. Jarvik, Susan Brandzel, Cassandra L. Neal, Sarah Li, Jason T. Gammack, Allen A. Gay, Ellen L. Goode, Leroy Hood, and Elaine A. Ostrander

354 **Evidence for a Familial Pregnancy-Induced Hypertension Locus in the eNOS-Gene Region**
Reynir Arngrímsson, Caroline Hayward, Sophie Nadaud, Ásdis Baldursdóttir, James J. Walker, Wang A. Liston, Ragnheiður I. Bjarnadóttir, David J. H. Brock, Reynir T. Geirsson, J. Michael Connor, and Florent Soubrier

363 **Localization of a Gene for Autosomal Dominant Osteopetrosis (Albers-Schönberg Disease) to Chromosome 1p21**
Wim Van Hul, Jens Bollerslev, Jeppe Gram, Els Van Hul, Wim Wuyts, Olivier Benichou, Filip Vanhoenacker, and Patrick J. Willems

370 **Localization of the Gene Causing Keratolytic Winter Erythema to Chromosme 8p22-p23, and Evidence for a Founder Effect in South African Afrikaans-Speakers**
Michelle Starfield, Hans Christian Hennies, Martin Jung, Trefor Jenkins, Thomas Wienker, Peter Hull, Amanda Spurdle, Wolfgang Küster, Michele Ramsay, and André Reis

379 **Identification of a Duplication of Xq28 Associated with Bilateral Periventricular Nodular Heterotopia**
James M. Fink, William B. Dobyns, Renzo Guerrini, and Betsy A. Hirsch

388 **Balanced Translocation 46,XY,t(2;15)(q37.2;q11.2) Associated with Atypical Prader-Willi Syndrome**
Jeffrey M. Conroy, Theresa A. Grebe, Laurie A. Becker, Karen Tsuchiya, Robert D. Nicholls, Karin Buiting, Bernhard Horsthemke, Suzanne B. Cassidy, and Stuart Schwartz

395 **A Submicroscopic Deletion in Xq26 Associated with Familial Situs Ambiguus**
Giovanni B. Ferrero, Marinella Gebbia, Giuseppe Pilia, David Witte, Andrea Peier, Robert J. Hopkin, William J. Craigen, Lisa G. Shaffer, David Schlessinger, Andrea Ballabio, and Brett Casey

402 **The Apo(a) Gene Is the Major Determinant of Variation in Plasma Lp(a) Levels in African Americans**
Vincent Mooser, Douglas Scheer, Santica M. Marcovina, Jinping Wang, Rudy Guerra, Jonathan Cohen, and Helen H. Hobbs

418 **Analysis of Genetic Linkage and Somatic Loss of Heterozygosity in Affected Pairs of First-Degree Relatives**
K. Rohde, M. D. Teare, and M. Santibáñez Koref

423 **Accurate Inference of Relationships in Sib-Pair Linkage Studies**
Michael Boehnke and Nancy J. Cox

430 **True and False Positive Peaks in Genomewide Scans: Applications of Length-Biased Sampling to Linkage Mapping**
Joseph D. Terwilliger, William D. Shannon, G. Mark Lathrop, John P. Nolan, Lynn R. Goldin, Gary A. Chase, and Daniel E. Weeks

439 **Tests for Linkage and Association in Nuclear Families**
E. R. Martin, N. L. Kaplan, and B. S. Weir

Letters to the Editor

449 **Hemizygous Deletion of the Syntaxin 1A Gene in Individuals with Williams Syndrome**
Lucy R. Osborne, Sylvia Soder, Xiao-Mei Shi, Barbara Pober, Teresa Costa, Stephen W. Scherer, and Lap-Chee Tsui

452 **Further Evidence Suggesting the Presence of a Locus, on Human Chromosome 5q31-q33, Influencing the Intensity of Infection with *Schistosoma mansoni***
Bertram Müller-Myhsok, Foekje F. Stelma, Fatou Guissé-Sow, Birgit Muntau, Thorsten Thye, Gerd D. Burchard, Bruno Gryseels, and Rolf D. Horstmann

454 **Multiple Sclerosis in Sardinia Is Associated and in Linkage Disequilibrium with HLA-DR3 and -DR4 Alleles**
Maria Giovanna Marrosu, Maria Rita Murru, Gianna Costa, Francesco Cucca, Stefano Sotgiu, Giulio Rosati, and Francesco Muntoni

458 **Nonrandom X-Chromosome Inactivation in Hemopoietic Cells from Carriers of Dyskeratosis Congenita**
Anna Maria Ferraris, Gian Luca Forni, Rosa Mangerini, and Gian Franco Gaetani

461 **Is There an Abnormal Phenotype Associated with Maternal Isodisomy for Chromosome 2 in the Presence of Two Isochromosomes?**
Lisa G. Shaffer, Christopher McCaskill, Catherine A. Egli, John C. Baker, and Kathreen M. Johnston

462 **Evidence for a Possible Asian Origin of YAP^+ Y Chromosomes**
Tasha K. Altheide and Michael F. Hammer

466 **Genetic Counseling Is Directive? Look Again**
Seymour Kessler

Book Review

468 ***Cancer Cytogenetics.* 2d ed.** By Sverre Heim and Felix Mitelman
Reviewed by Janet D. Rowley

Announcements

469 **Employment and Fellowship Opportunities; Workshop; Call for Proposals; Cell Cultures/DNA Available**

Erratum

471 **Localization of a Novel X-Linked Progressive Cone Dystrophy Gene to Xq27: Evidence for Genetic Heterogeneity,** by Bergen and Pinckers (June 1997 [60:1468–1478])

Information for Contributors

September 1997

i **This Month in the *Journal***
John Ashkenas

Editorial

473 **Bells and Whistles**
Peter H. Byers

Insights from Model Systems

475 **Semper Fidelis: What Man's Best Friend Can Teach Us about Human Biology and Disease**
Elaine A. Ostrander and Edward Giniger

481 **Of Monkeys and Men: Vervets and the Genetics of Human-Like Behaviors**
Roberta M. Palmour, John Mulligan, J. Jeffry Howbert, and Frank Ervin

489 **Baboons as an Animal Model for Genetic Studies of Common Human Disease**
Jeffrey Rogers and James E. Hixson

Invited Editorial

494 **HLA and Mate Selection in Humans: Commentary**
Gary K. Beauchamp and Kunio Yamazaki

Original Articles

497 **HLA and Mate Choice in Humans**
Carole Ober, Lowell R. Weitkamp, Nancy Cox, Harvey Dytch, Donna Kostyu, and Sherman Elias

505 **HLA and Mate Selection: No Evidence in South Amerindians**
Philip W. Hedrick and Francis L. Black

512 **Confirmation of a Double-Hit Model for the *NF1* Gene in Benign Neurofibromas**
Eduard Serra, Susana Puig, David Otero, Antonia Gaona, Helena Kruyer, Elisabet Ars, Xavier Estivill, and Conxi Lázaro

520 **Mutation Screening of the EXT1 and EXT2 Genes in Patients with Hereditary Multiple Exostoses**
Christophe Philippe, Daniel E. Porter, Mark E. Emerton, Dan E. Wells, A. Hamish R. W. Simpson, and Anthony P. Monaco

529 **Transglutaminase 1 Mutations in Autosomal Recessive Congenital Ichthyosis: Private and Recurrent Mutations in an Isolated Population**
Elina Laiho, Jaakko Ignatius, Hanna Mikkola, Vivien C. Yee, David C. Teller, Kirsti-Maria Niemi, Ulpu Saarialho-Kere, Juha Kere, and Aarno Palotie

539 **Autosomal Recessive Phosphorylase Kinase Deficiency in Liver, Caused by Mutations in the Gene Encoding the β Subunit (*PHKB*)**
Inge E. T. van den Berg , Ellen A. C. M. van Beurden, Johannis B. C. de Klerk, Otto P. van Diggelen, Helga E. M. Malingré, Marijke M. Boer, and Ruud Berger

547 A Spectrum of Mutations in the Second Gene for Autosomal Dominant Polycystic Kidney Disease (PKD2)
B. Veldhuisen, J. J. Saris, S. de Haij, T. Hayashi, D. M. Reynolds, T. Mochizuki, R. Elles, R. Fossdal, N. Bogdanova, M. A. van Dijk, E. Coto, D. Ravine, S. Nørby, C. Verellen-Dumoulin, M. H. Breuning, S. Somlo, and D. J. M. Peters

556 Deletion of *RB* Exons 24 and 25 Causes Low-Penetrance Retinoblastoma
Rod Bremner, Daisy Chan Du, Mary J. Connolly-Wilson, Peter Bridge, K. Farid Ahmad, Homa Mostachfi, Dianne Rushlow, James M. Dunn, and Brenda L. Gallie

571 Analysis of the *RPGR* Gene in 11 Pedigrees with the Retinitis Pigmentosa Type 3 Genotype: Paucity of Mutations in the Coding Region but Splice Defects in Two Families
Ricardo Fujita, Monika Buraczynska, Linn Gieser, Weiping Wu, Patricia Forsythe, Magnus Abrahamson, Samuel G. Jacobson, Paul A. Sieving, Sten Andréasson, and Anand Swaroop

581 The Molecular Pathology of Progressive Symmetric Erythrokeratoderma: A Frameshift Mutation in the Loricrin Gene and Perturbations in the Cornified Cell Envelope
Akemi Ishida-Yamamoto, John A. McGrath, HaMut Lam, Hajime Iizuka, Richard A. Friedman, and Angela M. Christiano

590 Characterization of Two Mutations Associated with Epimerase-Deficiency Galactosemia, by Use of a Yeast Expression System for Human UDP-Galactose-4-Epimerase
B. B. Quimby, A. Alano, S. Almashanu, A. M. DeSandro, T. M. Cowan, and J. L. Fridovich-Keil

599 Characterization of 18 New Mutations in COL7A1 in Recessive Dystrophic Epidermolysis Bullosa Provides Evidence for Distinct Molecular Mechanisms Underlying Defective Anchoring Fibril Formation
Alain Hovnanian, Ariane Rochat, Christine Bodemer, Elisabeth Petit, Caroline A. Rivers, Catherine Prost, Sylvie Fraitag, Angela M. Christiano, Jouni Uitto, Mark Lathrop, Yann Barrandon, and Yves de Prost

611 Maternal Uniparental Disomy of Chromosome 1 with Reduction to Homozygosity of the LAMB3 Locus in a Patient with Herlitz Junctional Epidermolysis Bullosa
Leena Pulkkinen, Florencia Bullrich, Paula Czarnecki, Lester Weiss, and Jouni Uitto

620 Molecular Definition of 22q11 Deletions in 151 Velo-Cardio-Facial Syndrome Patients
C. Carlson, H. Sirotkin, R. Pandita, R. Goldberg, J. McKie, R. Wadey, S. R. Patanjali, S. M. Weissman, K. Anyane-Yeboa, D. Warburton, P. Scambler, R. Shprintzen, R. Kucherlapati, and B. E. Morrow

630 Identification of a Locus for Progressive Familial Intrahepatic Cholestasis *PFIC2* on Chromosome 2q24
Sandra S. Strautnieks, Amir F. Kagalwalla, M. Stuart Tanner, A. S. Knisely, Laura Bull, Nelson Freimer, Sam A. Kocoshis, R. Mark Gardiner, and Richard J. Thompson

634 A New Rett Syndrome Family Consistent with X-Linked Inheritance Expands the X Chromosome Exclusion Map
N. Carolyn Schanen, E. Jill Roth Dahle, Fiorentino Capozzoli, Vanja A. Holm, Huda Y. Zoghbi, and Uta Francke

642 Chromosome 1p36 Deletions: The Clinical Phenotype and Molecular Characterization of a Common Newly Delineated Syndrome
Stuart K. Shapira, Christopher McCaskill, Hope Northrup, Aimee S. Spikes, F. F. B. Elder, V. Reid Sutton, Julie R. Korenberg, Frank Greenberg, and Lisa G. Shaffer

651 Meiotic Segregation, Recombination, and Gamete Aneuploidy Assessed in a t(1;10)(p22.1;q22.3) Reciprocal Translocation Carrier by Three- and Four-Probe Multicolor FISH in Sperm
Paul Van Hummelen, David Manchester, Xiu Lowe, and Andrew J. Wyrobek

660 **Screening and Diagnosis for the Fragile X Syndrome among the Mentally Retarded: An Epidemiological and Psychological Survey**
Bert B. A. de Vries , Ans M. W. van den Ouweland, Serieta Mohkamsing, Hugo J. Duivenvoorden, Esther Mol, Kirsten Gelsema, Monique van Rijn, Dicky J. J. Halley, Lodewijk A. Sandkuijl, Ben A. Oostra, Aad Tibben, and Martinus F. Niermeijer, for the Collaborative Fragile X Study Group

668 **Recessive Inheritance of Obesity in Familial Non–Insulin-Dependent Diabetes Mellitus, and Lack of Linkage to Nine Candidate Genes**
Sandra J. Hasstedt, Michael Hoffman, Mark F. Leppert, and Steven C. Elbein

678 **Interactions between Genetic and Reproductive Factors in Breast Cancer Risk in a French Family Sample**
N. Andrieu and F. Demenais

691 **Mitochondrial Footprints of Human Expansions in Africa**
Elizabeth Watson, Peter Forster, Martin Richards, and Hans-Jürgen Bandelt

705 **Multilocus Genotypes, a Tree of Individuals, and Human Evolutionary History**
Joanna L. Mountain and L. Luca Cavalli-Sforza

719 **Differential Structuring of Human Populations for Homologous X and Y Microsatellite Loci**
Rosaria Scozzari, Fulvio Cruciani, Patrizia Malaspina, Piero Santolamazza, Bianca Maria Ciminelli, Antonio Torroni, David Modiano, Douglas C. Wallace, Kenneth K. Kidd, Antonel Olckers, Pedro Moral, Luciano Terrenato, Nejat Akar, Raheel Qamar, Atika Mansoor, Syed Q. Mehdi, Gianfranco Meloni, Giuseppe Vona, David E. C. Cole, Wangwei Cai, and Andrea Novelletto

734 **Association Mapping of Disease Loci, by Use of a Pooled DNA Genomic Screen**
Lisa F. Barcellos, William Klitz, L. Leigh Field, Rose Tobias, Anne M. Bowcock, Ross Wilson, Mark P. Nelson, Jane Nagatomi, and Glenys Thomson

748 **Markov Chain Monte Carlo Segregation and Linkage Analysis for Oligogenic Models**
Simon C. Heath

Letters to the Editor

761 **Common *BRCA1* Variants and Transcriptional Activation**
Alvaro N. A. Monteiro, Avery August, and Hidesaburo Hanafusa

762 **The Significance of the 187G (H63D) Mutation in Hemochromatosis**
Ernest Beutler

765 **Autosomal Dominant Axenfeld-Rieger Anomaly Maps to 6p25**
Douglas B. Gould, Alan J. Mears, William G. Pearce, and Michael A. Walter

768 **The Genetic Clock and the Age of the Founder Effect in Growing Populations: A Lesson from French Canadians and Ashkenazim**
Damian Labuda, Ewa Ziętkiewicz, and Małgorzata Labuda

771 **Approximate Variance of the Standardized Measure of Gametic Disequilibrium *D'***
Carlos Zapata, Gonzalo Alvarez, and Carmen Carollo

774 **Transmission/Disequilibrium Tests for Multiallelic Loci**
Pak Sham

778 **Reply to Sham**
Norman L. Kaplan, E. R. Martin, and B. S. Weir

778 **Family Cell Lines Available for Research—An Endangered Resource?**
Åke Lernmark, George Eisenbarth, Lee Ducat, Henry A. Erlich, Denise Faustman, Noel K. Maclaren, Jurg Ott, M. Alan Permutt, Jin-Xiong She, and John Todd

Book Reviews

780 ***Principles and Practice of Medical Genetics.* 3d ed.** Edited by David L. Rimoin, J. Michael Connor, and Reed E. Pyeritz. Senior Advisory Editor, Alan E. H. Emery
Reviewed by Cynthia Curry

781 ***Optimizing Genetics Services in a Social, Ethical, and Policy Context: Suggestions from Consumers and Providers in the New England Regional Genetics Group (NERGG).*** By Dorothy C. Wertz and Robin Gregg
Reviewed by Pat Schnatterly

Announcements

782 **Employment and Fellowship Opportunities; Workshop; Bone-Marrow-Cell Availability**

Information for Contributors

October 1997

i **This Month in the *Journal***
John Ashkenas

Gene Therapy '97

785 **The Promise and Reality of Cancer Gene Therapy**
Simon J. Hall, Shu-Hsia Chen, and Savio L. C. Woo

790 **Message Therapy: Gene Therapy That Targets mRNA Sequence and Stability**
Karen F. Kozarsky and Larry A. Couture

Insights from Model Systems

795 **Cell-Cycle Regulation of Mammalian DNA Double-Strand-Break Repair**
Eric A. Hendrickson

Invited Editorials

801 **Unconventional Myosins, the Basis for Deafness in Mouse and Man**
Tama Hasson

806 **Fetal Cells in Maternal Circulation: Progress in Analysis of a Rare Event**
James D. Goldberg

810 **What Is Significant in Whole-Genome Linkage Disequilibrium Studies?**
Leonid Kruglyak

Original Articles

813 Mutation Profile of All 49 Exons of the Human Myosin VIIA Gene, and Haplotype Analysis, in Usher 1B Families from Diverse Origins
A. Adato, D. Weil, H. Kalinski, Y. Pel-Or, H. Ayadi, C. Petit, M. Korostishevsky, and B. Bonne-Tamir

822 PCR Quantitation of Fetal Cells in Maternal Blood in Normal and Aneuploid Pregnancies
Diana W. Bianchi, John M. Williams, Lisa M. Sullivan, Frederick W. Hanson, Katherine W. Klinger, and Anthony P. Shuber

830 Genome Scanning for Segments Shared Identical by Descent among Distant Relatives in Isolated Populations
L. Kathryn Durham and Eleanor Feingold

843 Renal Cystic Disease in Tuberous Sclerosis: Role of the Polycystic Kidney Disease 1 Gene
Julian R. Sampson, Magitha M. Maheshwar, Richard Aspinwall, Peter Thompson, Jeremy P. Cheadle, David Ravine, Sushmita Roy, Eric Haan, Jay Bernstein, and Peter C. Harris

852 Identification of Genetic Mutations in Japanese Patients with Fructose-1,6-Bisphosphatase Deficiency
Yoshiharu Kikawa, Manabu Inuzuka, Byun Young Jin, Satomi Kaji, Jun-ichi Koga, Yoshiki Yamamoto, Kazuro Fujisawa, Ikue Hata, Akio Nakai, Yosuke Shigematsu, Hideo Mizunuma, Akira Taketo, Mitsufumi Mayumi, and Masakatsu Sudo

862 The X-Linked Gene G4.5 Is Responsible for Different Infantile Dilated Cardiomyopathies
Patrizia D'Adamo, Lucia Fassone, Agi Gedeon, Emiel A. M. Janssen, Silvia Bione, Pieter A. Bolhuis, Peter G. Barth, Meredith Wilson, Eric Haan, Karen Helen Örstavik, Michael A. Patton, Andrew J. Green, Enrico Zammarchi, Maria Alice Donati, and Daniela Toniolo

868 Neonatal, Lethal Noncompaction of the Left Ventricular Myocardium Is Allelic with Barth Syndrome
Steven B. Bleyl, Brian R. Mumford, Victor Thompson, John C. Carey, Theodore J. Pysher, Thomas K. Chin, and Kenneth Ward

873 Genetic Heterogeneity in Familial Acute Myelogenous Leukemia: Evidence for a Second Locus at Chromosome 16q21-23.2
Marshall Horwitz, Kathleen F. Benson, Feng-Qian Li, John Wolff, Mark F. Leppert, Lynne Hobson, Marie Mangelsdorf, Sui Yu, Duncan Hewett, Robert I. Richards, and Wendy H. Raskind

882 Familial Glaucoma Iridogoniodysplasia Maps to a 6p25 Region Implicated in Primary Congenital Glaucoma and Iridogoniodysgenesis Anomaly
Tim Jordan, Neil Ebenezer, Ruth Manners, James McGill, and Shomi Bhattacharya

889 Familial Infantile Convulsions and Paroxysmal Choreoathetosis: A New Neurological Syndrome Linked to the Pericentromeric Region of Human Chromosome 16
Pierre Szepetowski, Jacques Rochette, Patrick Berquin, Charles Piussan, G. Mark Lathrop, and Anthony P. Monaco

899 Chorea-Acanthocytosis: Genetic Linkage to Chromosome 9q21
Justin P. Rubio, Adrian Danek, Caroline Stone, Richard Chalmers, Nicholas Wood, Christine Verellen, Xavier Ferrer, Alessandro Malandrini, Gian M. Fabrizi, Michela Manfredi, Jefferey Vance, Margaret Pericak-Vance, Robert Brown, Gabrielle Rudolf, Fabienne Picard, Elisa Alonso, Mitchell Brin, Andrea H. Németh, Martin Farrall, and Anthony P. Monaco

909 Linkage of Familial Dilated Cardiomyopathy with Conduction Defect and Muscular Dystrophy to Chromosome 6q23
David N. Messina, Marcy C. Speer, Margaret A. Pericak-Vance, and Elizabeth M. McNally

918 The Gene for Autosomal Dominant Craniometaphyseal Dysplasia Maps to Chromosome 5p and Is Distinct from the Growth Hormone–Receptor Gene
Peter Nürnberg, Sigrid Tinschert, Michal Mrug, Jochen Hampe, Clemens R. Müller, Eike Fuhrmann, Hans-Steffen Braun, and André Reis

924 A Novel Locus for Autosomal Dominant Nonsyndromic Hearing Loss, DFNA13, Maps to Chromosome 6p
M. R. Brown, M. S. Tomek, L. Van Laer, S. Smith, J. B. Kenyon, G. Van Camp, and R. J. H. Smith

928 Hereditary Geniospasm: Linkage to Chromosome 9q13-q21 and Evidence for Genetic Heterogeneity
P. R. Jarman, N. W. Wood, M. T. Davis, P. V. Davis, K. P. Bhatia, C. D. Marsden, and M. B. Davis

934 A Gene for X-Linked Optic Atrophy Is Closely Linked to the Xp11.4-Xp11.2 Region of the X Chromosome
Jacqueline J. M. Assink, Nel T. Tijmes, Jacoline B. ten Brink, Roelof-Jan Oostra, Frans C. Riemslag, Paulus T. V. M. de Jong, and Arthur A. B. Bergen

940 Evidence for at Least Eight Fanconi Anemia Genes
Hans Joenje, Anneke B. Oostra, Mario Wijker, Franca M. di Summa, Carola G. M. van Berkel, Martin A. Rooimans, Wolfram Ebell, Margreet van Weel, Jan C. Pronk, Manuel Buchwald, and Fré Arwert

945 Risk Reversals in Predictive Testing for Huntington Disease
Elisabeth Almqvist, Shelin Adam, Maurice Bloch, Anne Fuller, Philip Welch, Debbie Eisenberg, Don Whelan, David Macgregor, Wendy Meschino, and Michael R. Hayden

953 The Fate of Human Sperm-Derived mtDNA in Somatic Cells
Giovanni Manfredi, Dominic Thyagarajan, Lefkothea C. Papadopoulou, Francesco Pallotti, and Eric A. Schon

961 Deletion of All CGG Repeats Plus Flanking Sequences in FMR1 Does Not Abolish Gene Expression
Karen Grønskov, Helle Hjalgrim, Mia O. Bjerager, and Karen Brøndum-Nielsen

968 Evidence for a Major Gene Controlling Susceptibility to Tegumentary Leishmaniasis in a Recently Exposed Bolivian Population
A. Alcaïs, L. Abel, C. David, M. E. Torrez, P. Flandre, and J. P. Dedet

Letters to the Editor

980 The Myth of Bumpy Hunter-Gatherer Mismatch Distributions
Hans-Jürgen Bandelt and Peter Forster

983 Reply to Bandelt and Forster
Gunter Weiss, Arndt von Haeseler, and Svante Pääbo

983 mtDNA Mutation Rates—No Need to Panic
Vincent A. Macaulay, Martin B. Richards, Peter Forster, Kate E. Bendall, Elizabeth Watson, Bryan Sykes, and Hans-Jürgen Bandelt

986 Reply to Macauley et al.
Neil Howell and David Mackey

Announcements

991 Employment and Residency Opportunities; Meetings; Mutant Cell Repository Catalog; Database; Call for Specimens; Call for Patients

Information for Contributors

November 1997

i **This Month in the *Journal***
John Ashkenas

Somatic Genetics '97

995 **Loss of Heterozygosity or: How I Learned to Stop Worrying and Love Mitotic Recombination**
Jay A. Tischfield

1000 **"Mistakes Happen": Somatic Mutation and Disease**
Feng Qian and Gregory G. Germino

Insights from Model Systems

1006 **Understanding Human Cancer in a Fly?**
Maie A. R. St. John and Tian Xu

Invited Editorial

1011 **DNA Variation and Language Affinities**
Guido Barbujani

Original Articles

1015 **Human Genetic Affinities for Y-Chromosome p49a,f/*Taq*I Haplotypes Show Strong Correspondence with Linguistics**
E. S. Poloni, O. Semino, G. Passarino, A. S. Santachiara-Benerecetti, I. Dupanloup, A. Langaney, and L. Excoffier

1036 **The Role of *MMAC1* Mutations in Early-Onset Breast Cancer: Causative in Association with Cowden Syndrome and Excluded in *BRCA1*-Negative Cases**
Hui C. Tsou, David H.-F. Teng, Xiao Li Ping, Valeria Brancolini, Thaylon Davis, Rong Hu, Xiao Xun Xie, Alexandra C. Gruener, Carolina A. Schrager, Angela M. Christiano, Charis Eng, Peter Steck, Jurg Ott, Sean V. Tavtigian, and Monica Peacocke

1044 **Mutation Detection in the Repeated Part of the PKD1 Gene**
Jeroen H. Roelfsema, Lia Spruit, Jasper J. Saris, Peter Chang, Yves Pirson, Gert-Jan B. van Ommen, Dorien J. M. Peters, and Martijn H. Breuning

1053 **Mutation Characterization and Genotype-Phenotype Correlation in Barth Syndrome**
Jennifer Johnston, Richard I. Kelley, Annette Feigenbaum, Gerald F. Cox, Geeta S. Iyer, Vicky L. Funanage, and Roy Proujansky

1059 **Evidence That the Penetrance of Mutations at the RP11 Locus Causing Dominant Retinitis Pigmentosa Is Influenced by a Gene Linked to the Homologous RP11 Allele**
T. L. McGee, M. Devoto, J. Ott, E. L. Berson, and T. P. Dryja

1067 **Molecular Analysis of the Androgen-Receptor Gene in a Family with Receptor-Positive Partial Androgen Insensitivity: An Unusual Type of Intronic Mutation**
H. T. Brüggenwirth, A. L. M. Boehmer, S. Ramnarain, M. C. T. Verleun-Mooijman, D. P. E. Satijn, J. Trapman, J. A. Grootegoed, and A. O. Brinkmann

1078 **Progressive Ataxia Due to a Missense Mutation in a Calcium-Channel Gene**
Qing Yue, Joanna C. Jen, Stanley F. Nelson, and Robert W. Baloh

1088 Evidence for Locus Heterogeneity in Puerto Ricans with Hermansky-Pudlak Syndrome
Senator Hazelwood, Vorasuk Shotelersuk, Scott C. Wildenberg, David Chen, Fumino Iwata, Muriel I. Kaiser-Kupfer, James G. White, Richard A. King, and William A. Gahl

1095 Rufous Oculocutaneous Albinism in Southern African Blacks Is Caused by Mutations in the *TYRP1* Gene
P. Manga, J. G. R. Kromberg, N. F. Box, R. A. Sturm, T. Jenkins, and M. Ramsay

1102 De Novo Rearrangements Found in 2% of Index Patients with Spinal Muscular Atrophy: Mutational Mechanisms, Parental Origin, Mutation Rate, and Implications for Genetic Counseling
Brunhilde Wirth, Thorsten Schmidt, Eric Hahnen, Sabine Rudnik-Schöneborn, Michael Krawczak, Bertram Müller-Myhsok, Jutta Schönling, and Klaus Zerres

1112 Localization of the Congenital Dyserythropoietic Anemia II Locus to Chromosome 20q11.2 by Genomewide Search
P. Gasparini, E. Miraglia del Giudice, J. Delaunay, A. Totaro, M. Granatiero, S. Melchionda, L. Zelante, and A. Iolascon

1117 Genetic Linkage of Paget Disease of the Bone to Chromosome 18q
J. D. Cody, F. R. Singer, G. D. Roodman, B. Otterund, T. B. Lewis, M. Leppert, and R. J. Leach

1123 Familial Nontoxic Multinodular Thyroid Goiter Locus Maps to Chromosome 14q but Does Not Account for Familial Nonmedullary Thyroid Cancer
Graham R. Bignell, Federico Canzian, Maryam Shayeghi, Markus Stark, Yin Y. Shugart, Patrick Biggs, Jonathan Mangion, Rifat Hamoudi, Jacalyn Rosenblatt, Paul Buu, Sophie Sun, Sheldon S. Stoffer, David E. Goldgar, Giovanni Romeo, Richard S. Houlston, Steven A. Narod, Michael R. Stratton, and William D. Foulkes

1131 Familial Multiple-System Tauopathy with Presenile Dementia Is Localized to Chromosome 17
J. R. Murrell, D. Koller, T. Foroud, M. Goedert, M. G. Spillantini, H. J. Edenberg, M. R. Farlow, and B. Ghetti

1139 A Gene for Arthrogryposis Multiplex Congenita Neuropathic Type Is Linked to D5S394 on Chromosome 5qter
Mordechai Shohat, Rona Lotan, Nurit Magal, Tamar Shohat, Nathan Fischel-Ghodsian, Jerome I. Rotter, and Lutfi Jaber

1144 D4 Dopamine-Receptor (DRD4) Alleles and Novelty Seeking in Substance-Dependent, Personality-Disorder, and Control Subjects
J. Gelernter, H. Kranzler, E. Coccaro, L. Siever, A. New, and C. L. Mulgrew

1153 D-3-Hydroxyacyl-CoA Dehydratase/D-3-Hydroxyacyl-CoA Dehydrogenase Bifunctional Protein Deficiency: A Newly Identified Peroxisomal Disorder
Yasuyuki Suzuki, Ling Ling Jiang, Masayoshi Souri, Shoko Miyazawa, Seiji Fukuda, Zhongyi Zhang, Mizuho Une, Nobuyuki Shimozawa, Naomi Kondo, Tadao Orii, and Takashi Hashimoto

1163 Laboratory Policies and Practices for the Genetic Testing of Children: A Survey of the Helix Network
Dorothy C. Wertz and Philip R. Reilly

1169 Effect of Genetic Heterogeneity and Assortative Mating on Linkage Analysis: A Simulation Study
Catherine T. Falk

1179 Allele-Sharing Models: LOD Scores and Accurate Linkage Tests
Augustine Kong and Nancy J. Cox

1189 Detection of Gene-Environment Interactions in Joint Segregation and Linkage Analysis
W. James Gauderman and Cheryl L. Faucett

Letters to the Editor

1200 **CFTR Gene Mutations in Men with Bilateral Ejaculatory-Duct Obstruction and Anomalies of the Seminal Vesicles**
Dieter Meschede, Bernd Dworniczak, Hermann M. Behre, Sabine Kliesch, Mireille Claustres, Eberhard Nieschlag, and Jürgen Horst

1202 **Mutations in the *TIGR* Gene in Familial Primary Open-Angle Glaucoma in Japan**
Yasuyuki Suzuki, Shiroaki Shirato, Fumiko Taniguchi, Kunitoshi Ohara, Kiyomi Nishimaki, and Shigeo Ohta

1204 **Childhood Cancer and Neural Tube Defects**
Julian Little

1205 **Reply to Little**
Steven Narod

1205 **Lafora Progressive Myoclonus Epilepsy: Narrowing the Chromosome 6q24 Locus by Recombinations and Homozygosities**
Jesus Sainz, Berge A. Minassian, Jose M. Serratosa, Manyee N. Gee, Lise M. Sakamoto, Reza Iranmanesh, Saeed Bohlega, Robert J. Baumann, Steve Ryan, Robert S. Sparkes, and Antonio V. Delgado-Escueta

Announcements

1210 **Employment and Fellowship Opportunities; Meeting; Courses; Prize; On-Line Database**

Information for Contributors

December 1997

i **This Month in the *Journal***
John Ashkenas

Insights from Model Systems

1213 **Genomic Imprinting: A Chromatin Connection**
Robert Feil and Gavin Kelsey

Chromatin Dynamics '97

1220 **Dynamic Interrelationships between DNA Replication, Methylation, and Repair**
Keith D. Robertson and Peter A. Jones

1225 **Centromere DNA Dynamics: Latent Centromeres and Neocentromere Formation**
K. H. Andy Choo

Invited Editorial

1234 **PTEN: Sometimes Taking It Off Can Be Better than Putting It On**
Michael P. Myers and Nicholas K. Tonks

Original Articles

1239 **Cloning of the Human Carnitine-Acylcarnitine Carrier cDNA and Identification of the Molecular Defect in a Patient**
Marjan Huizing, Vito Iacobazzi, Lodewijk IJlst, Paul Savelkoul, Wim Ruitenbeek, Lambert van den Heuvel, Cesare Indiveri, Jan Smeitink, Frans Trijbels, Ronald Wanders, and Ferdinando Palmieri

1246 Mutations of the Fanconi Anemia Group A Gene (*FAA*) in Italian Patients
Maria Savino, Leonarda Ianzano, Pierluigi Strippoli, Ugo Ramenghi, Araxy Arslanian, Gian Paolo Bagnara, Hans Joenje, Leopoldo Zelante, and Anna Savoia

1254 Inherited Mutations in PTEN That Are Associated with Breast Cancer, Cowden Disease, and Juvenile Polyposis
Eric D. Lynch, Elizabeth A. Ostermeyer, Ming K. Lee, J. Fernando Arena, HanLee Ji, Jamie Dann, Karen Swisshelm, David Suchard, Patrick M. MacLeod, Stener Kvinnsland, Bjorn Tore Gjertsen, Ketil Heimdal, Herb Lubs, Pål Møller, and Mary-Claire King

1261 Novel Alleles of the Chemokine-Receptor Gene *CCR5*
Mary Carrington, Teri Kissner, Bernard Gerrard, Sergey Ivanov, Stephen J. O'Brien, and Michael Dean

1268 Isolation and Chromosomal Localization of a Cornea-Specific Human Keratin 12 Gene and Detection of Four Mutations in Meesmann Corneal Epithelial Dystrophy
Kohji Nishida, Yoichi Honma, Atsuyoshi Dota, Satoshi Kawasaki, Wakako Adachi, Takahiro Nakamura, Andrew J. Quantock, Hisashi Hosotani, Shuji Yamamoto, Masaki Okada, Yoshikazu Shimomura, and Shigeru Kinoshita

1276 Splicing Defects in the *COL3A1* Gene: Marked Preference for 5′ (Donor) Splice-Site Mutations in Patients with Exon-Skipping Mutations and Ehlers-Danlos Syndrome Type IV
Ulrike Schwarze, Jayne A. Goldstein, and Peter H. Byers

1287 Spectrum of Mutations in the *RPGR* Gene That Are Identified in 20% of Families with X-Linked Retinitis Pigmentosa
Monika Buraczynska, Weiping Wu, Ricardo Fujita, Kinga Buraczynska, Ellen Phelps, Sten Andréasson, Jean Bennett, David G. Birch, Gerald A. Fishman, Dennis R. Hoffman, George Inana, Samuel G. Jacobson, Maria A. Musarella, Paul A. Sieving, and Anand Swaroop

1293 Molecular Analysis of the *NF2* Tumor-Suppressor Gene in Schwannomatosis
Lee B. Jacoby, Deborah Jones, Kevin Davis, David Kronn, M. Priscilla Short, James Gusella, and Mia MacCollin

1303 Variable Levels of a Heteroplasmic Point Mutation in Individual Hair Roots
Kate E. Bendall, Vincent A. Macaulay, and Bryan C. Sykes

1309 Human Phenylalanine Hydroxylase Mutations and Hyperphenylalaninemia Phenotypes: A Metanalysis of Genotype-Phenotype Correlations
Emre Kayaalp, Eileen Treacy, Paula J. Waters, Susan Byck, Piotr Nowacki, and Charles R. Scriver

1318 Mutations in *PDX1*, the Human Lipoyl-Containing Component X of the Pyruvate Dehydrogenase–Complex Gene on Chromosome 11p1, in Congenital Lactic Acidosis
Bernard Aral, Chantal Benelli, Ghania Ait-Ghezala, Mohamed Amessou, Françoise Fouque, Catherine Maunoury, Nicole Créau, Pierre Kamoun, and Cécile Marsac

1327 Peutz-Jeghers Syndrome: Confirmation of Linkage to Chromosome 19p13.3 and Identification of a Potential Second Locus, on 19q13 4
Hamid Mehenni, Jean-Louis Blouin, Uppala Radhakrishna, Shiv Shanker Bhardwaj, Kamla Bhardwaj, V. B. Dixit, Kent F. Richards, Ambrosio Bermejo-Fenoll, Antonio Silva Leal, Ranjan C. Raval, and Stylianos E. Antonarakis

1335 Localization of the Gene for Thiamine-Responsive Megaloblastic Anemia Syndrome, on the Long Arm of Chromosome 1, by Homozygosity Mapping
Ellis J. Neufeld, Hanna Mandel, Tal Raz, Raymonde Szargel, Chandri N. Yandava, Amy Stagg, Sabine Fauré, Timothy Barrett, Neil Buist, and Nadine Cohen

1342 Inherited Interstitial Duplications of Proximal 15q: Genotype-Phenotype Correlations
C. E. Browne, N. R. Dennis, E. Maher, F. L. Long, J. C. Nicholson, J. Sillibourne, and J. C. K. Barber

1353 **Skewed X-Chromosome Inactivation Is Common in Fetuses or Newborns Associated with Confined Placental Mosaicism**
Aster W. Lau, Carolyn J. Brown, Maria Peñaherrera, Sylvie Langlois, Dagmar K. Kalousek, and Wendy P. Robinson

1362 **Fragile X Premutations Are Not a Major Cause of Early Menopause**
Aileen Kenneson, Daniel W. Cramer, and Stephen T. Warren

1370 **Genetic Segregation Analysis of Early-Onset Recurrent Unipolar Depression**
Mary L. Marazita, Katherine Neiswanger, Margaret Cooper, George S. Zubenko, Donna E. Giles, Ellen Frank, David J. Kupfer, and Barry B. Kaplan

1379 **Genomewide Scan of Multiple Sclerosis in Finnish Multiplex Families**
Satu Kuokkanen, Michele Gschwend, John D. Rioux, Mark J. Daly, Joseph D. Terwilliger, Pentti J. Tienari, Juhani Wikström, Jorma Palo, Lincoln D. Stein, Thomas J. Hudson, Eric S. Lander, and Leena Peltonen

1388 **Use of a Quantitative Trait to Map a Locus Associated with Severity of Positive Symptoms in Familial Schizophrenia to Chromosome 6p**
L. M. Brzustowicz, W. G. Honer, E. W. C. Chow, J. Hogan, K. Hodgkinson, and A. S. Bassett

1397 **Linkage of Bipolar Affective Disorder to Chromosome 18 Markers in a New Pedigree Series**
Francis J. McMahon, Penelope J. Hopkins, Jianfeng Xu, Melvin G. McInnis, Sarah Shaw, Lon Cardon, Sylvia G. Simpson, Dean F. MacKinnon, O. Colin Stine, Robin Sherrington, Deborah A. Meyers, and J. Raymond DePaulo

1405 **Autosomal Dominant Postaxial Polydactyly, Nail Dystrophy, and Dental Abnormalities Map to Chromosome 4p16, in the Region Containing the Ellis–van Creveld Syndrome Locus**
Timothy D. Howard, Alan E. Guttmacher, Wendy McKinnon, Mridula Sharma, Victor A. McKusick, and Ethylin Wang Jabs

1413 **Diversity and Age of the Four Major mtDNA Haplogroups, and Their Implications for the Peopling of the New World**
Sandro L. Bonatto and Francisco M. Salzano

1424 **Genomewide Transmission/Disequilibrium Testing—Consideration of the Genotypic Relative Risks at Disease Loci**
Nicola J. Camp

1431 **Comparison of Nonparametric Statistics for Detection of Linkage in Nuclear Families: Single-Marker Evaluation**
Sean Davis and Daniel E. Weeks

Letters to the Editor

1445 **Instability of the $(CTG)_n$ Repeat in Congenital Myotonic Dystrophy**
Lee-Jun C. Wong and Tetsuo Ashizawa

1448 **Homogeneity of Kerato-Epithelin Codon 124 Mutations in Japanese Patients with Either of Two Types of Corneal Stromal Dystrophy**
Yukihiko Mashima, Yutaka Imamura, Minako Konishi, Akemi Nagasawa, Masakazu Yamada, Yoshihisa Oguchi, Jun Kudoh, and Nobuyoshi Shimizu

1450 **Identification of an Interstitial Deletion in an Adult Female with Schizophrenia, Mental Retardation, and Dysmorphic Features: Further Support for a Putative Schizophrenia-Susceptibility Locus at 5q21-23.1**
Robin L. Bennett, Maria Karayiorgou, Christina A. Sobin, Tom H. Norwood, and Mark A. Kay

1454 Meiotic Microdeletion Breakpoints in the BRCA1 Gene Are Significantly Associated with Symmetric DNA-Sequence Elements
Beatrice Schmucker and Michael Krawczak

1456 *Goosecoid*-Like Sequences and the Smallest Region of Deletion Overlap in DiGeorge and Velocardiofacial Syndromes
Antonella Pragliola, Vesna Jurecic, Cuc K. Chau, Nicole Philip, and Antonio Baldini

1458 Reply to Pragliola et al.
S. Gottlieb, B. S. Emanuel, and M. L. Budarf

1459 The Frequency of the Methylenetetrahydrofolate Reductase–Gene Mutation Varies with Age in the Normal Population
Sachio Matsushita, Taro Muramatsu, Hiroyuki Arai, Toshifumi Matsui, and Susumu Higuchi

Book Reviews

1461 *Pharmacogenetics.* By Wendell W. Weber. New York: Oxford University Press, 1997. Pp. 344. $60.00.
Daniel W. Nebert

1462 *Oxford Medical Databases,* version 2.0. By Robin Winter and Michael Baraitser. Oxford: Oxford University Press, 1996. £395.00 each.
J. M. Friedman

Announcements

1464 Employment and Fellowship Opportunities; Courses; Aging-Cell Repository; Somatic-Cell Hybrid Mapping Panel; Tissue Resource; Career Development Program

Errata

1468 Cancer Risks in Two Large Breast Cancer Families Linked to BRCA2 on Chromosome 13q12-13
Easton et al. (July 1997 [61:120–128])

1468 Characterization of 18 New Mutations in COL7A1 in Recessive Dystrophic Epidermolysis Bullosa Provides Evidence for Distinct Molecular Mechanisms Underlying Defective Anchoring Fibril Formation
Hovnanian et al. (September 1997 [61:599–610])

1468 Family Cell Lines Available for Research—An Endangered Resource?
Lernmark et al. (September 1997 [61:778–779])

1469 Editorial Reviewers for 1997

1474 Author Index for Volume 61

1482 Subject Index for Volume 61

1491 Contents of Volume 61

Information for Contributors